Native kidney biopsies in Armenian and Swiss children: high prevalence of amyloidosis in Yerevan and of IgA nephropathy in Zurich

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ORIGINAL ARTICLE

Native kidney biopsies in Armenian and Swiss children: high prevalence of amyloidosis in Yerevan and of IgA nephropathy in Zurich

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Abstract The spectrum of pathology in native kidney biopsies varies considerably between different countries. Based on similar biopsy policy and joint workup, biopsy data of native kidneys of children in Yerevan (Armenia) and Zurich (Switzerland) were compared over a period of two decades (1993–2002 and 2003–2012). A total of 487 renal biopsies in Yerevan (EVN), n=253; median age 11.2 years (range 0.8–18; 56 % males) and in Zurich (ZRH), n=234; median age 8.7 years (range 0.1–18; 61 % males) were analyzed. Biopsies from EVN were locally analyzed by light microscopy (LM) and sent to ZRH for electron microscopy (EM) and immunohistochemistry. Biopsies from ZRH were evaluated by LM, EM, and immunofluorescence. The significant difference concerns the high frequency of amyloidosis in EVN (25.4 % in the first and 19.4 % in the second decade vs. 0 % in ZRH) and of IgA nephropathy in ZRH (30.2 % in the first and 26.1 % in the second decade vs. 8.1 in EVN). Certain forms of glomerulonephritis (membranoproliferative type I and membranous) and primary focal segmental glomerulosclerosis tended to be more frequent in EVN than in ZRH. Amyloid nephropathy due to familial Mediterranean fever is still highly frequent in Armenia with a slight decrease in the second decade. In Switzerland, the most common finding was IgA nephropathy.

Keywords Amyloidosis · Epidemiology · Glomerulonephritis · IgA nephropathy · Native kidney · Renal biopsy

Introduction

The diagnosis of many kidney diseases in children is still based on renal biopsy despite the advances in imaging and genetic diagnostics and is essential for treatment and prognosis. Only limited data are available on indication and histological spectrum of renal biopsy findings in children regarding the comparison of different countries, ethnic groups, time periods, and children and adults [1–12]. More studies are available regarding adult patients only, some evaluating a large number of native kidney biopsies [13–16].

Following the earthquake of December 1988 in Armenia, percutaneous renal biopsy was established in Yerevan (EVN) in a partnership program with Zurich (ZRH). The renal biopsy policy was similar at both sites, and most biopsies from EVN (except mainly those with amyloidosis) were also evaluated in ZRH.

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The aims of this study were (1) to compare biopsy findings of both countries and (2) to look for trends over two decades.

Material and methods

From 1993 to 2012, 267 and 235 children underwent percutaneous native kidney biopsy in EVN (including five autopsies) and ZRH, respectively. Fourteen biopsies from EVN and one from ZRH containing insufficient material were excluded, resulting in a total of 487 eligible biopsies, with 253 from EVN (141 boys and 112 girls; median age 11.2 years, range 0.8–18) and 234 from ZRH (142 boys and 92 girls; median age 8.7 years, range 0.1–18). The children's hospitals in EVN and ZRH serve each a pediatric population (<18 years) of approximately 800,000.

The clinical indications for renal biopsies were

(1) Nephrotic syndrome (steroid-resistant, associated with hematuria and/or hypertension, impaired renal function or extrarenal symptoms)
(2) Persistent marked proteinuria (>1.0 g/m^2 per day)
(3) Persistent hematuria and proteinuria (<1.0 g/m^2 per day)
(4) Recurrent (≥3) episodes of gross, non-urological hematuria
(5) Acute kidney injury of unknown origin
(6) Only in Armenia: abnormal urinary findings in patients with known familial Mediterranean fever (FMF). FMF was diagnosed on history, clinical findings, and genetic analysis.

The observation time of 20 years with 487 biopsies was divided into two periods:

– Period I (1993–2002; n=210); n=114 for EVN, n=96 for ZRH
– Period II (2003–2012; n=277); n=139 for EVN, n=138 for ZRH

Biopsies from EVN were first processed by light microscopy (LM) in EVN; 183 of them were additionally examined in ZRH by LM, immunohistochemistry (IH, since 2005), and electron microscopy (EM). Biopsies from ZRH were evaluated by LM, immunofluorescence (IF), and EM.

Renal biopsy processing

For light microscopy, biopsy specimens from ZRH were fixed in 4 % buffered formalin and processed routinely. Biopsies from EVN were fixed in glutaraldehyde from 1993 to 2004 and in buffered formalin since 2005. Serial 2-μm-thick sections were cut and stained with hematoxylin and eosin, methenamine silver, periodic acid-Schiff reagent, elastic van Gieson, and acid fuchsin orange G-stain.

For immunofluorescence study, standard techniques were applied to frozen sections using fluorescein isothiocyanate-conjugated antisera to IgG, IgA, IgM, κ, and λ light chains, C3, C1q (Dako, Glostrup, Denmark) as well as α3 and α5 type IV collagen (Euro Diagnostica, Malmö, Sweden).

For immunohistochemistry on paraffin sections, standard procedures were applied using the Ventana BenchMark automated staining system with IgG, IgA, IgM, C3, and AA amyloid antibodies (Dako, Glostrup, Denmark).

For transmission electron microscopy, the biopsy was fixed in 2.5 % buffered glutaraldehyde, embedded in epon after postfixation with osmium tetroxide. Semithin sections were stained with methylene blue/azur II. Ultrathin sections were stained with uranyl acetate and lead citrate. The probes were examined using a Hitachi H-7650 TEM (Tokyo, Japan).

Statistical analysis was performed using unpaired t test for independent groups. A p value <0.05 was considered statistically significant. The study was approved by the local ethical committee.

Results

Clinical findings

The main clinical findings leading to a renal biopsy are shown in Table 1. Significantly more patients in EVN than in ZRH were nephrotic (p<0.001). However, the largest subgroup of nephrotic patients in EVN had FMF as the underlying disease. Among the 80 Armenian patients with FMF and proteinuria, 47 were nephrotic. If all 80 patients with FMF are excluded from analysis, the proportion of nephrotic syndrome (34.7 %) is closer to the corresponding data from ZRH (25.6 %).

Renal biopsy findings

The most frequent histological diagnosis (Table 2) found in *Armenia* was renal amyloidosis secondary to FMF, affecting 56 patients (22.1 %). The remaining 24 patients with known FMF had other renal involvement than amyloidosis. Renal amyloidosis was followed by focal segmental glomerulosclerosis (FSGS, 13.4 %) and minimal change nephrotic syndrome (MCNS, 10.3 %). Examples of renal biopsy findings in patients with and without FMF are shown in Fig. 1. In *ZRH*, the most frequent diagnosis was IgA nephropathy (IgAN; 27.8 %), either isolated (18.8 %) or associated with Henoch-Schönlein purpura (HSP; 9.0 %), followed by MCNS (10.7 %) and FSGS (9.8 %). Only one child was clinically and genetically diagnosed with FMF, however, the histology showed no amyloidosis, but FSGS.

Table 1 Clinical findings. Armenian patients with familial Mediterranean fever (FMF) are listed separately

Main clinical findings	Yerevan (n=253)		Zurich (n=234)
Nephrotic syndrome (NS)	107 (42 %)		60 (26 %)
	FMF excluded n=173	FMF detected n=80	
Steroid-resistant	38	–	34
Steroid-sensitive, but dependant	3	–	6
NS combined with hematuria and/or renal insufficiency	15	–	15
NS in patients with other extrarenal symptoms	4	–	4
NS in patients with FMF (familial Mediterranean fever)	–	47	1
Non-nephrotic patients	146 (58 %)		174 (74 %)
Urinary abnormality (proteinuria±hematuria)	50	25	102
Nephritic syndrome	28	3	34
Acute kidney injury	9	1	14
Rapidly progressive GN	18	2	15
Chronic renal insufficiency	8	2	9

Table 2 Renal pathology. Percentages for Yerevan are shown for all patients and after exclusion of FMF. Significantly higher percentages (p<0.05) in Yerevan or Zurich are italicized

Histology	Yerevan (EVN)				Zurich (ZRH)	
	All patients		Excluding FMF patients		All patients	
	n	%	n	%	n	%
Amyloidosis	56	*22.1*	80	0	0	0
Minimal change nephrotic syndrome (MCNS)	26	10.3	18	10.4	25	10.7
Focal segmental glomerulosclerosis (FSGS)	34	13.4	30	*17.3*	23	9.8
Diffuse mesangial sclerosis (DMS)	3	1.2	3	1.7	6	2.6
Acute postinfectious glomerulonephritis (APGN)	13	5.1	7	4	13	5.6
Membranoproliferative GN type I (MPGN I)	15	5.9	14	8.1	8	3.3
Dense deposit disease (DDD)	6	2.4	6	3.5	6	2.6
C3-glomerulonephritis	0	0	0	0	3	1.3
Membranous nephropathy (MN)	12	4.7	12	*6.9*	4	1.7
IgA nephropathy (IgAN)	12	4.7	10	5.8	44	*18.8*
IgAN associated with Henoch-Schönlein purpura (HSP)	9	3.6	8	4.6	21	*9.0*
Systemic lupus erythematosus (SLE)	19	7.5	19	*11.0*	10	4.3
Thrombotic microangiopathy (TMA), hemolytic uremic syndrome (HUS)	8	3.3	8	4.6	10	4.3
Vasculitis ANCA-associated	3	1.2	3	1.7	8	3.3
Thin basement membrane disease (TBMD)	7	2.8	6	3.5	14	6.0
Alport syndrome	15	5.9	15	*8.7*	5	2.1
Acute tubular necrosis (ATN)	0	0	0	0	8	3.4
Tubulointerstitial nephritis (TIN)	2	0.8	1	0.6	6	2.6
Other	2 [a]	0.8	2	1.2	10 [b]	4.3
No pathology	0	0	0	0	6	2.6
Not diagnostic	11	4.3	11	6.4	4	1.7
Total	253	100	173	100	234	100

[a] One patient each with nephronophthisis and lymphoma

[b] One patient each with nephronophthisis, Joubert syndrome, renal-hepatic-pancreatic dysplasia, tubular dysgenesis, Finnish type nephrotic syndrome, lymphoma, C1q-nephropathy, arteriolar hyalinosis, and two patients with Fabry disease

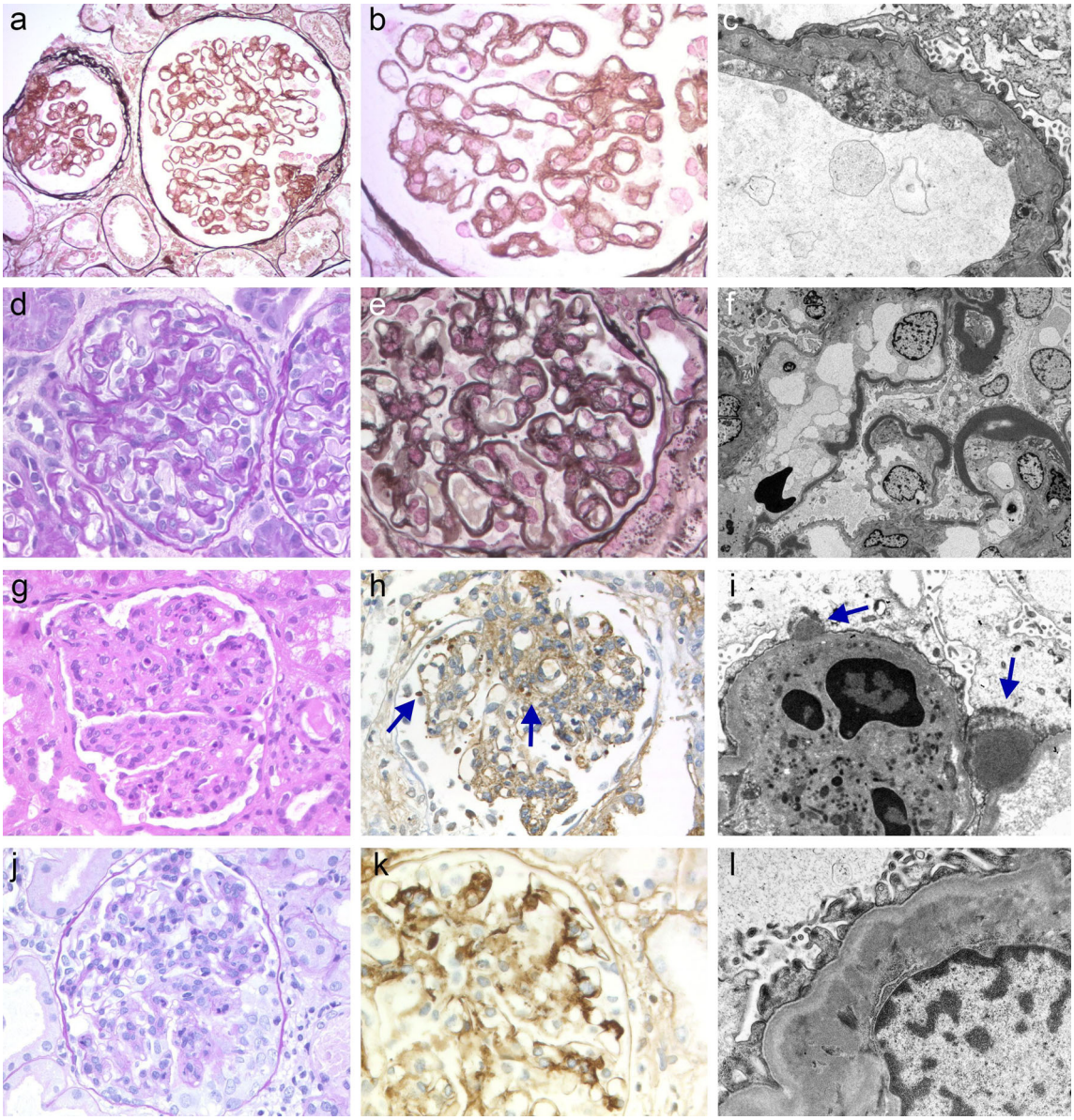

Fig. 1 Examples of renal biopsy findings in biopsies from EVN after exclusion of FMF (**a**–**c** NS, **d**–**e** no NS) and in FMF (**g**–**i** NS, **j**–**l** no NS). **a**–**c** Alport syndrome: **a** segmental sclerotic lesions, **b** irregularities of the glomerular basement membrane (GBM) with splitting, **c** splitting and multilamellation of the GBM (**a**–**b** methenamine silver, original magnification **a** ×200, **b** ×400, **c** TEM, original magnification ×13,500). **d**–**f** Dense deposit disease: **d**–**e** thickened, glassy GBM, **f** highly osmiophilic dense deposits in the GBM (**d** periodic acid-Schiff reagent, original magnification ×240, **e** methenamine silver, original magnification ×240, **f** TEM, original magnification ×1950). **g**–**i** Postinfectious glomerulonephritis: **g** endocapillary proliferation, **h** C3-positive chunky subepithelial deposits (→), **i** subepithelial "humps" (→) (**g** hematoxylin and eosin, original magnification ×160, **h** C3 immunostaining, original magnification ×200, **i** TEM, original magnification ×5800). **j**-**l** IgA nephropathy: **j** mesangial and endocapillary proliferation and a cellular crescent, **k** IgA-positive mesangial deposits, **l** mesangial electron dense deposits (**j** periodic acid-Schiff reagent, original magnification ×160, **k** IgA immunostaining, original magnification ×320, **l** TEM, original magnification ×4000)

Comparison between Yerevan and Zurich

As expected, amyloidosis secondary to FMF was the most frequent renal pathology (22.1 %) in EVN. In contrast, no amyloidosis was diagnosed in ZRH. This disease is very specific for some ethnic groups (Armenians, non-Ashkenazi Jews, Arabs, Turks) and extremely rare in Europe. The age at onset of FMF was 3.2±3 years (range 0.3–14) and the age at biopsy was 12.0±3.9 years (range 5–18). Forty-four of the 47 nephrotic patients with FMF from EVN had amyloidosis, two had MCNS, and one had FSGS. Out of the 33 non-nephrotic patients with FMF, 12 had amyloidosis, six each had MCNS and acute postinfectious glomerulonephritis (APGN), three had FSGS, two had isolated IgAN, and one each had

membranoproliferative glomerulonephritis type I (MPGN I), HSP, thin basement membrane disease (TBMD), and tubulointerstitial nephritis.

In order to allow a closer comparison, both series were further analyzed after exclusion of the Armenian patients with FMF (Table 2). In contrast to renal amyloidosis, IgAN was seen significantly more often in ZRH than in EVN, particularly the isolated form ($p<0.001$). IgAN associated with HSP tended also to be more frequent in ZRH. Glomerulonephritis (GN) secondary to systemic lupus erythematosus (SLE) was more prevalent in EVN than in ZHR ($p<0.05$); 15 of the 19 Armenian patients were females. MPGN I, membranous nephritis (MN; $p<0.05$) and the Alport syndrome ($p<0.01$) were seen more often in EVN than in ZRH. Two patients from ZRH were diagnosed with C3 glomerulonephritis, in one of them the diagnosis was made by re-biopsy.

Comparison between the two time periods (Figs. 2a, b)

The proportion of patients showing IgAN in EVN increased from 6.1 to 10.1 %, mainly due to isolated IgAN (Fig. 2a). However, IgAN (both isolated and associated with HSP) was observed far more often in ZRH and has remained the most prevalent diagnosis despite a minor decline from 30.2 % in the first to 26.1 % in the second decade (Fig. 2b).

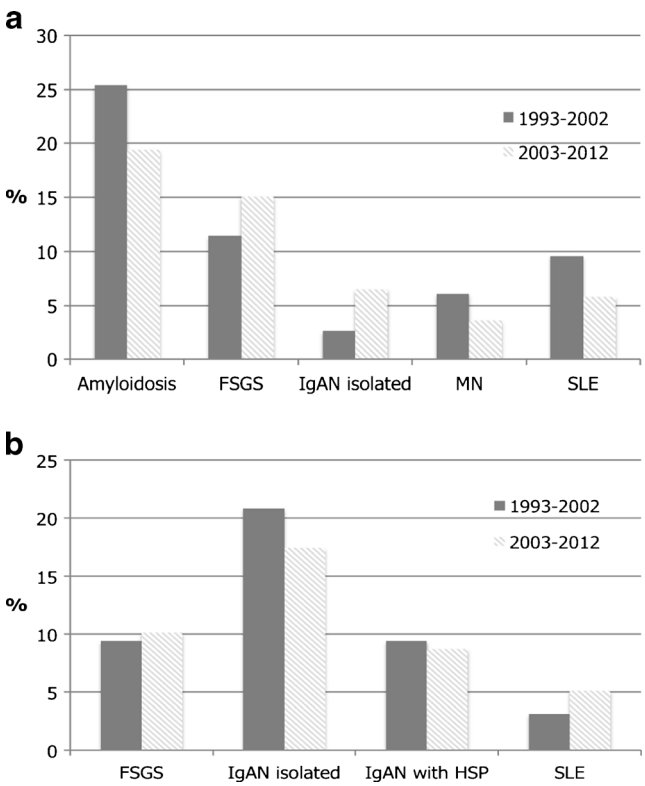

Fig. 2 **a** Comparison of selected diagnoses in two decades in *Yerevan* (as % of all patients per period). **b** Comparison of selected diagnoses in two decades in *Zurich* (as % of all patients per period)

Only in EVN, a trend was observed suggesting an increase of patients with FSGS, which however did not reach statistical significance (calculated as *t* test). In contrast, the percentage of patients with amyloidosis slightly decreased, but the absolute number of patients (29 versus 27) remained largely unchanged.

Discussion

This study provides data on renal biopsy findings in pediatric patients of two different countries. Of special interest is the direct comparison, made possible by similar policy for performing renal biopsies and by biopsy evaluation at the same pathology service.

The most obvious difference concerns the very large number of patients in EVN suffering from renal amyloidosis due to FMF. This is an unusual proportion, even in countries with a large number of FMF. For example, not a single patient with amyloidosis has been reported in Saudi Arabia among 128 children with the nephrotic syndrome [1]. FMF constitutes in fact a major health problem in Armenia with a carrier rate being as high as 1:5 [17]. Renal amyloidosis is largely a preventable condition, if FMF is diagnosed early and colchicine is administered regularly. The alarmingly high number of patients with amyloidosis in our series is due to the absence of systematic prophylactic measures until 2002 as a result of the economic crisis and major disturbances of the health care in Armenia.

However, even with established amyloidosis some nephrotic patients may go into partial or even full remission after administration of colchicine, but the response is not predictable [18]. As compared to the first period, there was a slight decline in the second period (2003–2012) and it is expected that the number of renal amyloidosis will considerably decrease over the next years.

Apart of amyloidosis, some other renal diseases have been observed in patients with FMF, as FMF is known to be weakly associated with various forms of GN, but in at least MCNS, FSGS, and APGN, it was probably coincidental. Nevertheless, it is known that FMF predisposes to different types of vasculitis (e.g., polyarteritis nodosa, HSP), often with serious renal lesions and rapid progression [19–21]. A special group comprises 12 FMF patients with proteinuria or the nephrotic syndrome without hematuria—thus mimicking amyloid nephropathy—were found to have MCNS or FSGS.

A considerably higher proportion of patients with IgAN (either isolated or associated with HSP) was observed in ZRH as compared to EVN. The question arises whether IgAN and HSP are really more frequent in ZRH. Although biopsies from EVN were not examined by IH till 2005, we do not think that isolated IgAN was grossly

underdiagnosed in EVN. In fact, histological findings as mesangial proliferation, mesangial electron dense deposits without hump-like subepithelial or intramembranous highly dense deposits allow a presumptive diagnosis of IgAN in the context of hematuria, even without IF or IH [22]. Another reason explaining the lower number of IgAN in EVN, particularly during the first time period, is the late referral rate of patients. In contrast to isolated IgAN, diagnosis of HSP is based on clinical symptoms, and in general, no renal biopsy was done if renal function remained normal. The number of patients requiring renal biopsies may strongly fluctuate, as has been demonstrated in ZRH. In the literature, the frequency of IgAN among pediatric biopsies strongly depends on study design and the corresponding health care system. There is a rather lower rate in the USA or Europe [23] compared with countries as Korea or Japan, where a considerably higher proportion of IgAN is diagnosed most often initiated by general mass school urine screening [6, 24].

The number of biopsies in APGN was similar in both countries, although over 600 pediatric patients were seen in EVN during the study period [25]. However, a renal biopsy is rarely needed since the course of APGN in children is usually self-limited.

The true incidence of MCNS is far higher than diagnosed in our study, as the indication for biopsy was limited to steroid-resistant nephrotic syndrome. If biopsies are performed in all nephrotic children, the incidence of MCNS is reported to be higher [10].

Our data do not demonstrate an increasing trend of FSGS during the last two decades, as had been suggested not only in adults [14, 15], but also in children [26].

The lower number of MPGN I in ZRH as compared to EVN could be an effect of the overall decrease of MPGN I observed over the last few decades in adult patients, first in industrialized and later in developing countries [13, 27]. The larger number of biopsies showing SLE in EVN might be real, as the prevalence of SLE is likely to be higher in Armenia than in Central Europe [28].

This study only included biopsy-proven renal diseases and therefore does not reflect the whole spectrum of pediatric renal disorders. Indeed, some hereditary renal disorders are diagnosed by genetic analysis (e.g., autosomal dominant polycystic kidney disease, cystinosis, Dent's disease, Lowe syndrome).

In conclusion, the present study allows a direct comparison between renal biopsy findings of two countries and two different time periods. The most obvious finding was the high incidence of amyloidosis secondary to FMF in Armenia, whereas IgAN was more prevalent in Zurich. Considerable differences between the first and the second observation decades have been observed for certain glomerular diseases. While the proportion of IgAN in Armenia increased, a decreasing trend of patients with amyloidosis was observed.

Conflict of interest All authors shall disclose possible conflicts of interest after publication.

References

1. Al-Rasheed SA, Al-Mugeiren MM, Al-Salloum AA, Al-Sohaibani MO (1996) Childhood renal diseases in Saudi Arabia. A clinicopathological study of 167 cases. Int Urol Nephrol 28:607–613
2. Bhimma R, Coovadia HM, Adhikari M (1997) Nephrotic syndrome in South African children: changing perspectives over 20 years. Pediatr Nephrol 11:429–434
3. Coppo R, Gianoglio B, Porcellini MG, Maringhini S (1998) Frequency of renal diseases and clinical indications for renal biopsy in children (report of the Italian National Registry of Renal Biopsies in Children). Group of Renal Immunopathology of the Italian Society of Pediatric Nephrology and Group of Renal Immunopathology of the Italian Society of Nephrology. Nephrol Dial Transplant 13:293–297
4. Piqueras AI, White RH, Raafat F, Moghal N, Milford DV (1998) Renal biopsy diagnosis in children presenting with haematuria. Pediatr Nephrol 12:386–391
5. McKinney PA, Feltbower RG, Brocklebank JT, Fitzpatrick MM (2001) Time trends and ethnic patterns of childhood nephrotic syndrome in Yorkshire, UK. Pediatr Nephrol 16:1040–1044
6. Utsunomiya Y, Koda T, Kado T, Okada S, Hayashi A, Kanzaki S, Kasagi T, Hayashibara H, Okasora T (2003) Incidence of pediatric IgA nephropathy. Pediatr Nephrol 18:511–515
7. Nammalwar BR, Vijayakumar M, Prahlad N (2006) Experience of renal biopsy in children with nephrotic syndrome. Pediatr Nephrol 21:286–288
8. Yuen LK, Lai WM, Lau SC, Tong PC, Tse KC, Chiu MC (2008) Ten-year review of disease pattern from percutaneous renal biopsy: an experience from a paediatric tertiary renal centre in Hong Kong. Hong Kong Med J 14:348–355
9. Miller M, Gooden M, Shah D, Soyibo AK, Williams J, Barton EN (2010) Renal biopsy findings in Jamaican children. West Indian Med J 59:325–329
10. Absar A, Diamond M, Sonia Y, Arshalooz R, Safia A, Waqar K, Shahid P (2010) Ten year experience of pediatric kidney biopsies from a single center in Pakistan. Indian J Nephrol 20:190–192
11. Briganti EM, Dowling J, Finaly HPA, Jones CL, Kincaid-Smith PS, Sinclair R, McNeil JJ, Atkins RC (2001) The incidence of biopsy-proven glomerulonephritis in Australia. Nephrol Dial Transplant 16: 1364–1367
12. Rychlik I, Jancova E, Tesar KA, Lacha J, Stejskal J, Stejskalova A, Dusek J, Herout V (2004) The Czech registry of renal biopsies. Occurrence of renal diseases in the years 1994–2000. Nephrol Dial Transplant 19:3040–3049
13. Narasimhan B, Chacko B, John GT, Korula A, Kirubakaran MG, Jacob CK (2006) Characterization of kidney lesions in Indian adults: towards a renal biopsy registry. J Nephrol 19:205–210
14. Swaminathan S, Leung N, Lager DJ, Melton LJ, Bergstralh EJ, Rohlinger A, Fervenza FC (2006) Changing incidence of glomerular disease in Olmsted County, Minnesota: a 30-year renal biopsy study. Clin J Am Soc Nephrol 1:483–487
15. Malafronte P, Mastroianni-Kirsztajn G, Betonico GN, Romao JE Jr, Alves MA, Carvalho MF, Viera Neto OM, Cadaval RA, Bergamo RR, Woronik V, Sens YS, Marrocos MS, Barros RT (2006) Paulista

Registry of glomerulonephritis: 5-year data report. Nephrol Dial Transplant 21:3098–3105
16. Woo KT, Chan CM, Chin YM, Choong HL, Tan HK, Foo M, Anantharaman V, Lee GS, Chiang GS, Tan PH, Lim CH, Tan CC, Lee E, Hb T, Fook-Chong S, Lau YK, Wong KS (2010) Global evolutionary trend of the prevalence of primary glomerulonephritis over the past three decades. Nephron Clin Pract 116:c337–346
17. Sarkisian T, Ajrapetian H, Beglarian A, Shahsuvarian G, Egiazarian A (2008) Familial Mediterranean fever in Armenian population. Georgian Med News 156:105–111
18. Sarkissian A, Papazian M, Sanamyan A, Leumann E (2000) Colchicine in the treatment of renal amyloidosis secondary to familial Mediterranean fever. Nephrol Dial Transplant 15:1098
19. Tekin M, Yalçinkaya F, Tümer N, Cakar N, Koçak H, Ozkaya N, Gençgönül H (1999) Familial Mediterranean fever—renal involvement by diseases other than amyloid. Nephrol Dial Transplant 14: 475–479
20. Akpolat T, Akpolat I, Karagoz F, Yilmaz E, Kandemir B, Ozen S (2004) Familial Mediterranean fever and glomerulonephritis and review of the literature. Rheumatol Int 24:43–45
21. Aksu K, Keser G (2011) Coexistence of vasculitides with familial Mediterranean fever. Rheumatol Int 31:1263–1274
22. Ferrario F, Rastaldi MP (2004) Histopathological atlas of renal diseases—IgA nephropathy. J Nephrol 17:351–353
23. McGrogan A, Franssen CFM, de Vries CS (2011) The incidence of primary glomerulonephritis worldwide: a systematic review of the literature. Nephrol Dial Transplant 26:414–430
24. Park YH, Choi JY, Chung HS, Koo JW, Kim SY, Namgoong MK, Park YS, Yoo KH, Lee KY, Lee DY, Lee SJ, Lee JE, Chung WY, Hah TS, Cheong HI, Choi Y, Lee KS (2005) Hematuria and proteinuria in a mass school urine screening test. Pediatr Nephrol 20:1126–1130
25. Sarkissian A, Papazian M, Azatian G, Arikiants N, Babloyan A, Leumann E (1997) An epidemic of acute postinfectious glomerulonephritis in Armenia. Arch Dis Child 77:342–344
26. Srivastava T, Simon SD, Alon US (1999) High incidence of focal segmental glomerulosclerosis in nephrotic syndrome of childhood. Pediatr Nephrol 13:13–18
27. Zhou FD, Zhao MH, Zou WZ, Liu G, Wang H (2009) The changing spectrum of primary glomerular diseases within 15 years: a survey of 3331 patients in a single Chinese centre. Nephrol Dial Transplant 24: 870–876
28. Huang JL, Yao TC, See LC (2004) Prevalence of pediatric systemic lupus erythematosus and juvenile chronic arthritis in a Chinese population: a nation-wide prospective population-based study in Taiwan. Clin Exp Rheumatol 22:776–780